REMARKS

Claims 1-72 are pending and were subject to restriction. Claims 7, 9, 14-16, 34-42, 71 and 72 have been withdrawn from consideration. Examined claims 1-6, 8, 10-13, 17-33 and 43-70 stand variously rejected under 35 U.S.C. §§ 112, first and second paragraphs, 102 and 103. In addition, these claims are provisionally rejected under the judicially created doctrine of obviousness-type double patenting. Applicants reserve the right to file one or more continuing applications directed to the subject matter of these claims during the pendency of this application.

Independent claims 1 and 43 have been amended herein to make explicit what was previously implicit. In particular, it is now clarified that a component of a chromatin remodeling complex is a subunit protein of a multiprotein chromatin remodeling complex (or functional fragment of the subunit), as described throughout the specification, for example on page 24, lines 16-22. Further, these claims have also been amended to specify that fusion molecule comprising a DNA binding domain and subunit of a chromatin remodeling complex alters chromatin structure, as described throughout the specification as filed. Claim 8 has been amended to properly depend from amended claim 1 and claim 5 has been amended to correct a typographical error. No new matter has been added as a result of these amendments and entry thereof is respectfully requested.

Request to Withdraw Finality

Applicants respectfully request that the Office withdraw the finality of this Office Action and issue another non-final Office Action in this case. This request is made because the newly presented rejections were not necessitated by Applicants' previous amendments.

As indicated in M.P.E.P. 706.07(a), final rejection is not proper when it is neither necessitated by Applicants' amendments nor based on information submitted in an IDS. In the pending case, the allegedly new rejections are based on a reference (Verdine) previously cited by the Office under 35 U.S.C. § 103 (now cited under §§ 102/103) and on a reference (Peterson) previously considered by the Office in an IDS. (See, IDS mailed May 1, 2002, an initialed copy of which accompanied the first Office Action). Furthermore, Applicants' previous amendments made in the paper filed on April 11, 2003, did not affect the Office's ability to apply the same references in the previous Office Action. Therefore, there is absolutely no reason that the rejections newly-presented in the Office Action mailed July 2, 2003 could not have been made previously. In other words, Applicants' amendments did **not** necessitate the newly presented

rejections. Accordingly, Applicants herein request that the outstanding Office Action be considered non-final and this response treated accordingly.

Double Patenting

Claims 1-6, 8, 10-13, 17-33 and 43-70 stand provisionally rejected under 35 U.S.C. § 101 as allegedly claiming the same invention as that of claims 1-15 and 17-20 of copending application no. 09/942,087. (Office Action, paragraph 12).

As previously noted in Applicants' response dated April 11, 2003, and as explicitly set forth in the claims as amended above, the pending claims are all directed to methods in which a subunit protein (or functional fragment thereof) of a chromatin remodeling complex is used in a first fusion molecule to alter chromatin structure, not to regulate gene expression. (See, also, Remarks below regarding rejection under 35 U.S.C. §102 for a discussion of the difference between altering chromatin structure and regulation of gene expression). In contrast, the cited portions of the 09/942,087 application are directed to methods in which a DNMT protein is used as a functional domain for repression of transcription. Thus, the pending claims are not obvious over this application and withdrawal of the obviousness-type double patenting rejection is respectfully requested.

Rejections Under 35 U.S.C. § 112, Written Description

Claims 1-6, 8, 10-13, 17-33 and 43-70 stand rejected as allegedly containing subject matter that was not described in the specification as filed. (Final Office Action, paragraph 15).

Applicants again submit that the term "component," as defined in the specification as filed, related to polypeptides only and, accordingly, is not overly broad and direct the Office's attention to page 24, lines 19-21 of the specification, where it is stated:

> A component of a chromatin remodeling complex can comprise **one of its constituent proteins** or a functional fragment thereof. (emphasis added)

In addition, Applicants note that page 49, line 25 through page 51, line 7; and Examples 6, 8, 9 and 10, for example, disclose a number of assays for chromatin remodeling, which would allow one of skill in the art to determine whether any given protein was or was not a component (*i.e.*, subunit protein) of a chromatin remodeling complex, are provided in the specification.

Nonetheless, in an effort to advance prosecution, the claims have been amended to remove the term "component" and replace it with terms that set forth further structure and nature

of the claimed chromatin remodeling polypeptides. Accordingly, the foregoing amendments obviate this rejection and withdrawal thereof is requested.

Rejections Under 35 U.S.C. § 112, Second Paragraph

Claims 1-6, 8, 10-13, 17-33 and 43-70 stand rejected as allegedly indefinite. (Office Action, paragraphs 19-20). In particular, the metes and bounds of the terms "component," are allegedly not known.

Applicants believe that one of skill in the art would readily understand that the term "component of a chromatin remodeling complex" refers a polypeptide present in a multiprotein chromatin remodeling complex. *See*, for example, Cairns (1998) *Trends Biochem. Sci.* **23:**20-25, especially at page 21, first column, second full paragraph, wherein it is stated: "The yeast complex RSC (remodels the structure of chromatin) contains 15 **polypeptides**, and several **components** of RSC are strikingly similar to **components** of SWI-SNF."[1] (emphasis added) *See* also Knoepfler *et al.* (1999) *Cell* **99:**447-450, sentence bridging pages 448 and 449, wherein it is stated: "Both of these **proteins**, as well as the recently identified MBD3 **protein** . . . appear to be integral **components** of the Mi-2/NuRD complex . . ."[2] (emphasis added). *See* also Workman *et al.* (1998) *Ann. Rev. Biochem.* **67:**545-579, in particular page 569, first full paragraph, second sentence, wherein it is stated: "Deletion of genes that encode **components** of the SWI/SNF complex is not lethal to growth, whereas deletion of RSC **components** is lethal."[3] (emphasis added and noting that it is well known to those of skill in the art that genes encode proteins).

Despite the clarity of this term as originally presented, the foregoing amendments to claims 1 and 43 obviate the rejection, which should therefore be withdrawn.[4]

Rejections Under 35 U.S.C. § 102

Claims 1-5, 8, 10, 12, 13, 17, 18 and 68-70 stand rejected under 102(e) as allegedly anticipated by U.S. Patent No. 6,183,965 (hereinafter "Verdine"). (Office Action, paragraph 23).

As a threshold matter, Applicants disagree with the Office's assertion that transcriptional modulation is equivalent to chromatin remodeling. (*See, e.g.,* paragraph 23 in which a chromatin remodeling complex is cited as being used a transcriptional modulator). In fact, transcriptional modulation and altering of chromatin structure are separate processes distinguished, for example,

[1] Reference AP-1 of IDS mailed on May 1, 2002
[2] Reference BJ-1 of IDS mailed on May 1, 2002
[3] Reference DB-1 of IDS mailed on May 1, 2002
[4] The Office has acknowledged that the term "functional fragments thereof" is definite when used with respect to proteins (paragraph 17 of the Final Office Action). Therefore, any concern about this term has also been obviated by the amendments herein.

on page 4, lines 1-7 of the specification as filed. Because of these differences, Verdine's disclosure of transcriptional modulators does not anticipate the claimed methods, all of which involve alteration of chromatin structure.

Moreover, Applicants' methods involve the use of a fusion molecule comprising a DNA binding domain and a subunit of a chromatin remodeling complex (or functional fragment thereof). Verdine, on the other hand, requires that the DNA binding domain and the chromatin remodeling complex be contained on separate molecules -- **not** together in a chimeric protein as the Office has asserted in paragraph 23. Indeed, Verdine's system necessitates that, when used, a protein that interacts with a chromatin remodeling complex (a "transcriptional modulator" in his terms) should be fused to a ligand (not to a DNA binding domain). In turn, the ligand must recognize a chimeric DNA binding-ligand binding protein and the complex of the two chimeric molecules must modulate gene expression. (*See, e.g.,* claim 1 of Verdine). This is clearly an entirely different method than claimed by Applicants.

Since Verdine in no way describes, demonstrates or suggests each and every aspect of the methods as claimed, withdrawal of the rejection is respectfully requested.

Rejections Under 35 U.S.C. § 103

Claims 1-5, 8, 10, 12, 13, 17-22, 27-30, 43-45, 47, 51-53, 56, 59 and 68-70 stand newly rejected under 103(a) as allegedly obvious over Verdine in view of U.S. Patent No. 5,972,608 (hereinafter "Peterson"). (Final Office Action, paragraph 26). In addition, claims 1-6, 8, 10, 12, 13, 17-33 and 43-70 stand rejected as allegedly obvious over Verdine in view of Peterson and in further view of Cardoso and Omichinski. (Final Office Action, paragraph 27). Finally, claims 1-6, 8, 10-13, 17-33 and 43-70 stand rejected as allegedly obvious over Verdine in view of Peterson and further in view of Cardoso and Omichinski and further in view of Rutter. (Final Office Action, paragraph 28).

For the reasons set forth above, the primary reference (Verdine) does not teach or suggest the methods as claimed. Verdine is directed entirely toward methods of modulating gene expression (which are not equivalent to methods of altering chromatin structure). Verdine's methods require that a chimeric DNA binding-ligand binding molecule interact with a separate chimeric ligand-transcriptional modulatory molecule. Nowhere does this reference suggest that a fusion of a DNA binding protein and a subunit protein of chromatin remodeling complex could function on its own to alter chromatin structure (claims 1-33 and 68-70) or in combination with a second molecule to modulate gene expression (claims 43-67).

The secondary references do not supply what is missing from Verdine. Peterson is directed to assays and reagents for chromatin remodeling enzymes and is entirely silent as to DNA binding molecules. Further, claim 43 and claims depending therefrom do not, as suggested by the Office, require the use of two chromatin remodeling enzymes. (Final Office Action, first paragraph on page 15). Rather, these claims are directed to methods of modulating gene expression by contacting cellular chromatin with a first fusion molecule that alters chromatin structure and a second molecule that modulates gene expression. Neither Verdine nor Peterson teach or suggest such methods or DNA binding-chromatin remodeling complex fusion molecules. Therefore, the rejection of claims 1-5, 8, 10, 12, 13, 17-22, 27-30, 43-45, 47, 51-53, 56, 59 and 68-70 as allegedly obvious over Verdine in view of Peterson should be withdrawn.

For their parts, Cardoso, Omichinski and Rutter contain no teachings or suggestions regarding methods of altering the structure of cellular chromatin as claimed. Indeed, Cardoso is concerned with analyzing the XNP gene product while Omichinski relates to elucidation of the structure and mode of binding a GAGA-factor DNA complex. Rutter relates to a single polymorphism in MMR and, as such, contains no suggestion to arrive at the methods as claimed.

In sum, there is no combination of the cited references that would reasonably lead one of skill in the art to the claimed subject matter, must less any motivation to combine the cited references. Therefore, Applicants respectfully request that the rejections be withdrawn.

CONCLUSION

Applicants respectfully submit that the claims are in condition for allowance. If the Examiner notes any further matters which the Examiner believes may be expedited by a telephone interview, the Examiner is requested to contact the undersigned.

Respectfully submitted,

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